

Update on Implementation of Recommendations of the Guidelines Harmonization Working Group

Clinical Trials and Translational Research Advisory
Committee (CTAC)

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Guidelines Harmonization Working Group: GOALS

- Harmonize program guidelines and develop incentives to foster collaboration among all components of the clinical trials infrastructure including Cancer Centers, SPOREs, and Cooperative Groups
- Promote collaborative team science:
 - Ensure that guidelines for different clinical trials funding mechanisms are aligned
 - Eliminate redundancy and duplication while proactively encouraging collaboration

Guidelines Harmonization Working Group: Approach

- Define collaboration
- Identify model collaborative efforts
- Examine current guidelines for clinical & translational research infrastructures and disincentives to collaboration
- Develop a vision document with recommendations
- Present to CTAC (July 2009)

Guidelines Harmonization Working Group: Recommendations

- **Revise Guidelines**
 - Describe collaborative efforts across mechanisms in specified section of application
 - Provide meaningful guidance on what is needed to receive credit for collaboration across NCI translational and clinical trials system.
 - Credit should be reflected in priority score.
 - Incentivize trans-mechanism collaborations that will move novel interventions from pre-clinical to early clinical to phase III trials.

Guidelines Harmonization Working Group: Recommendations

- **Incentives to Collaboration (1)**
 - Salary Support and individual investigator recognition
 - Institutional Cooperative Group PIs
 - Expand institutional U10s
 - Mechanisms to enhance recognition & career development for those who contribute to collaborative clinical trials efforts – but are not PIs
 - Collaborative efforts to enhance patient accrual
 - Per patient reimbursement
 - Credit for accrual to trials led by others
 - Increase CTSU capacity to accommodate CC and SPORE trials

Guidelines Harmonization Working Group: Recommendations

- **Incentives to Collaboration (2)**
 - Formalize process to facilitate collaborations between non-Cooperative Group study teams and Cooperative Groups.
 - Evaluate effectiveness of Grants for Coordination of Clinical/Translational Research (Grand Opportunities, GO, Grants) with intent of possible mechanism for long term support of similar grants

Guidelines Harmonization Working Group: Recommendations

- **Outcomes Measures - Using CTWG, TRWG evaluation process, measure progress in collaboration**
 - Consistent guidelines across mechanisms that promote collaboration
 - Review credit reflected in priority scores
 - Collaborative activities between programs
 - Phase III trials based on early phase studies
 - Increased contributions by program leaders across translational/clinical trials system

Guidelines Harmonization Recommendations NCI Implementation Team

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Implementation of Recommendations (Proposed)

- Progress:
 - Recommendations of GHWG and OEWG were “mapped” to SPORE, Cancer Center, and Cooperative Group guidelines
 - Draft “harmonized” guideline revisions proposed for
 - SPOREs
 - Cancer Center Support Grants
 - Cooperative Groups
 - Incentives to Collaboration
 - Programs in early implementation and/or development

Key Proposed Guidelines Revisions

Collaborations across clinical trials & translational science mechanisms

- Separate sections in SPORE, Cooperative Group Guidelines
- Integrated into multiple sections in Cancer Center Guidelines

Incentives to Collaboration

- Enhance recognition & career development for individuals who make substantive contributions to clinical trials efforts
 - Cancer Clinical Investigator Team Leadership Award
- Coordination of Clinical/Translational Research Across the NCI {Grand Opportunities (GO) Grants}
 - Evaluate projects funded under ARRA for possible expansion of initiative

Incentives to Collaboration

- Organ Site Specific Meetings
 - Goal: foster collaborations, create objectives & outcomes aligned with scientific priorities of the organ site
 - stimulate the movement of translational science into clinical trials
- Formalize a process to support Collaborative Multi-Center Phase II Trials led by NCI-designated Cancer Centers and SPOREs
 - Announcement published November 2010

<http://ccct.cancer.gov/files/CTSUSHarmonizationAnnouncement.pdf>

CTSU/Harmonization Opportunity

Purpose:

Encourage collaborations and “hand-offs” (bench to bedside and back) between Cooperative Group, Cancer Center, and SPORE investigators through Steering Committee (SC) discussions on clinical trial concepts

Opportunities:

- SPORE and NCI Designated Cancer Center Investigators bring ideas for clinical trials or components (e.g., biomarkers) to SCs for input and collaborations → merits “review credit” under new guidelines
- Support for CTSU services for Phase 2 treatment trials reviewed & approved by SC, CTROC

CTSU/Harmonization Opportunity

- Support available for up to two treatment trials in FY2011
- Phase 2 randomized, multi-center treatment trials (min. 4 accrual sites)
- SPORE or Cancer Center PI with ≥ 100 and < 200 total patients
- Collaboration with another SPORE, Cancer Center, or Cooperative Group
- Consideration for trials that cannot be led by one or more Cooperative Groups, e.g., network with access to CTSU or other multi-center trial coordination support

CTSU can provide: Regulatory support, Website document hosting , Protocol coordination , Patient registration, Study coordination, Clinical database development, Data management , Data processing , Information, technology, Site accrual support.

Not available: Investigational New Drug (IND) application and statistical support, data safety monitoring, auditing services

Incentives to Collaboration

- Recommendations requiring further consideration:
 - Increase or provide support of PIs, other investigators for collaboration across mechanisms on clinical trials development & implementation
 - Expand U10 grants to qualifying institutions that participate in clinical trials
 - Utilize K-type awards to tailor an award to senior investigators for salary support for facilitation of collaborations across programs
 - Increase per patient reimbursement for participation in clinical trials

Guideline Harmonization Revisions: SPOREs

- Collaborative research has *always* been a key feature of the SPOREs: both in the guidelines and in review (**Program Organization and Capabilities "POC" Section**).
- Until 1/10 submissions, POC was a reviewed, but not written section. Now both a written AND a reviewed section.
- POC has 7 review elements including Collaborations.
- Collaborations element is being removed and will be placed in a new independent section: **"Scientific Collaboration" (SC)** that will receive a separate score.
- The previous 70%:30% weighting for overall impact (priority score) will be eliminated.
 - Reviewers will focus on the translational impact of the proposed research projects as they are supported by the shared cores in the context of the POC, the SC, and the developmental programs of the SPORE.

Scientific Collaboration (SC) Section to include:

- Description of collaborative efforts that have as their goal moving cancer therapeutic, biomarker, prevention or epidemiological studies from the discovery/laboratory phase to early clinical trials/studies to later phase studies and beyond.
 - Within the SPORE community
 - Across NCI-supported clinical trial and translational science mechanisms
 - With other government and non-government programs
- Description of leadership related to collaboration.
- Description of collaborative arrangements, where appropriate, such as separate grants, contracts, or CRADAs with industry, for the continued development of SPORE concepts.

The Scientific Collaboration Section

Definitions:

- **Horizontal Collaboration**: Collaboration in which groups work together coordinately to accomplish a set of research aims or goals on a single level, that is, in the laboratory, or at the clinical trial stage, or as a population clinical study.
- **Vertical Collaboration**: Collaboration in which groups work together sequentially or with some overlap, to move up the translational research pathway, that is, from discovery, to pre-clinical development, to Phase I trials or studies, to later phase studies, and possibly to a final hand-off to a commercial company.

Each SPORE must demonstrate a commitment to both *horizontal* and *vertical* collaboration in completing preclinical projects and moving promising results along the pathway of translational/clinical development.

The Scientific Collaboration Section

- **New** SPORE applications
 - are expected to set out plans for any future horizontal and/or vertical collaborations for *direct* translational projects that will eventually reach a clinical study, and for translational projects in the *reverse* direction, such as projects in biomarker discovery and development, that will eventually require analytical and clinical validation
- **Renewal** SPORE applications
 - are expected to describe for any prior, current, or proposed projects, where appropriate: (1) planned, ongoing, and/or completed **horizontal** collaborative projects and programs with set milestones and explain how the joint efforts will further the translational goals of the SPORE; and (2) the accomplishments of any **vertical** collaborations where promising SPORE results were handed off to other NCI-supported clinical trial mechanisms or to non-governmental mechanisms.

Vertical Collaboration Possibilities in the SPOREs

- Only Phase I and early Phase II (<100 patients) clinical trials may be supported by the SPORE without collaboration.
- For collaboration with other SPOREs, Cancer Centers, and other NCI grant mechanisms, on randomized Phase II therapeutic trials (≥ 100 patients), SPOREs should use the appropriate **NCI Disease Specific Steering Committees and their Task Forces** working together to develop clinical concepts from early SPORE trials that could move forward to the Clinical Trials Cooperative Groups. Collaborative concepts may also include correlative studies.
- An alternative, but limited, collaborative opportunity for large Phase II trials is access to the **NCI Cancer Trials Support Unit (CTSU)** resources upon recommendation by a Disease Specific Steering Committee when it is not possible to use the Clinical Trial Cooperative Groups. Additional information can be obtained from the Coordinating Center for Clinical Trials staff.

Final Notes

- A clinical trial may not be the goal of many SPORE projects.
- These projects will often reach a human endpoint by studying patients' specimens to expand upon observations or outcomes in the clinic, a process known as "reverse translation."
- However, when biomarker studies are ready for clinical trials, SPOREs are encouraged to collaborate with trans-NCI clinical trial mechanisms to validate the biomarkers.

Implementation

SPORES Tentative Timeline



Key Proposed Guidelines Revisions Cancer Centers

- Approach to Guidelines Revisions
 - The P30 Cancer Center Support Grant mechanism supports a broad mission, encompassing the entire spectrum of cancer research
 - Harmonization of guidelines across the clinical trials enterprise is part of a larger effort to foster collaboration and integration across that spectrum
 - GHWG recommendations are embedded into existing Guidelines components
 - Over 40 reviewed elements in existing Guidelines
 - Impact greater by incorporating into existing elements that drive the priority score

Key Proposed Guidelines Revisions Cancer Centers

- Elements Modified
 - 6 Essential Characteristics: Transdisciplinary Coordination and Collaboration
 - New emphasis on how the Center facilitates movement of findings through translational pipeline, with emphasis on coordination across NCI mechanisms
 - Senior Leadership
 - New focus on how the Center leadership develops/implements collaborative strategies that advance scientific findings
 - Recognition of Clinical Staff
 - Expanded language to encourage program membership and recognize clinical contributions
 - Support of Clinical Staff Investigators (continuing)

Key Proposed Guidelines Revisions Cancer Centers

- Elements Modified (cont.)
 - Clinical and Translational Programs
 - New emphasis on:
 - Activating, and accruing to, a diverse portfolio of clinical trials **having potential impact for patients**
 - Initiating and moving forward pilot and early phase studies that capitalize on the centers scientific strengths
 - Transitioning findings through the translational continuum through coordination across NCI and other funding mechanisms and other collaborative partnerships
 - Leadership of, and accrual to, Cooperative Group trials
 - 2nd stage Comprehensiveness Review
 - Greater emphasis on clinical training programs, dissemination

Implementation

CANCER CENTERS

Tentative Timeline



Key Proposed Guidelines Revisions Cooperative Groups

Cooperative Groups:

- Provide high value in review for meaningful participation (accrual) to intergroup trials
- Define meaningful participation in intergroup studies (e.g., at least 5-10% of total accrual for a trial, depending on size of the Group)
- Provide high value in review for innovative collaborations with NCI-funded early clinical trials mechanisms

Key Proposed Guidelines Revisions Cooperative Groups

Cooperative Groups:

- Evidence of leadership & accrual to intergroup trials led by other Cooperative Groups
- Evidence of collaborations with other NCI-funded mechanisms to move novel interventions through translational /clinical continuum

Next Steps

- Incorporate revisions and other guidelines changes to move through the approval process
- Publish
- Implement guidelines revisions in review
- Assess impacts, outcomes



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